Attorney Reference No.: 59486.000002
Application No. 09/853,635
Filed: May 14, 2001
Applicant: Bengt Krister OLSON
Group Art Unit: 1655
Examiner: Dr. Kailash C. Srivastava
Date of Amendment: October 1, 2007

REMARKS

Telephone Interviews

Applicant's undersigned Counsel had two telephone interviews with the Examiner, on July 10 and 12, 2007. Applicant appreciates the Examiner's attention to this application matter and his helpful suggestions regarding claim language (as discussed below).

On July 10th, the Examiner contacted the Counsel and proposed that Applicant amend claim 104 by inserting into claim 104 one set of weight ratios from each of claims 134 and 135. The Examiner suggested that Applicant amend claims 134 and 135 by retaining one weight ratio in each claim, and add new claims directed to the remaining weight ratios. During the interview there was also a preliminary discussion of possibly amending claim 104 by changing "increasing collagen synthesis or lessening the decrease in collagen synthesis or lessening the decrease in collagen synthesis" to –stabilizing collagen synthesis--, and inserting into claim 104 the limitations from claim 114, but this alternative was dismissed. Counsel advised that he would relay the proposed amendment to the Applicant.

On July 12th, Counsel advised the Examiner that Applicant agreed with proposed amendment. However, the Examiner replied that, upon further consideration of Applicant's November 30, 2006 Amendment, he noticed several other issues hat need to be addressed in an Office Action, which he would issue.

Specification Amendments

Applicant amended specification at page 20, to render text, under the heading "Results" consistent. No new matter is introduced by these amendments.

Claim Amendments

Applicant amended claims 104, 112, 114, 115, 120, 124, 129-131, 134, 135, 137-139 and added new claims 140-149. Support for the claim amendments and new claims is found

in the application, considered as a whole, including original claims, and claims 134, 135. No new matter or new issues are introduced. In view of the interviews and due to the absence of new issues in the amended and new claims, entry of all amendments into the record is respectfully requested.

General Matters

In the Office Action, it was pointed out that Applicant's November 30, 2006 response miss-identified the mailing date of the Office Action to which it was responsive as "July 30, 2006". Applicant agrees with the Examiner that the mailing date of that Office Action was July 31, 2006, and expresses his regret for this inadvertent miss-identification of the date. Applicant authorizes the U.S. Patent and Trademark Office to make an appropriate correction to the record.

Restriction/Election

Applicant appreciates the Examiner's indication that Applicant has the option to file a petition challenging the propriety of the restriction requirement and its finality.

Claim Objections

Claim 104 was objected to because, allegedly it is not clear how one can make a distinction between natural and synthetic components for each of glycosaminoglycan and polyphenolic, hydrophilic antioxidant, recited in the claim, where the natural source for the components are enzymatic hydrolysate and grape seed, respectively. Office Action pages 4-5.

In response to Applicant's argument that persons of ordinary skill in the art would be readily able to make such differentiation, it was asserted that Applicant did not recite any known method for doing so, nor provided any documentary source for such method.

Applicant respectfully traverses this objection. At the outset, Applicant respectfully submits that the initial burden of denying patentability to a claimed invention rests upon the USPTO, e.g., *In re Piasecki*, 223 USPQ 785, 788 (CAFC 1984). Applicant submits that the

USPTO has not met this burden. The MPEP, Section 706.01 states that a claim may be properly objected to if its form (rather than substance) is improper. The USPTO has not provided any reason for the implied assertion that the form of claim 104 is not proper.

Furthermore, Applicant submits that artisans of ordinary skill in this art are not likely to have a need to distinguish between the natural and synthetic components. If the USPTO is aware of any particular reasons that such persons of ordinary skill will need to differentiate between natural and synthetic components, Applicant would appreciate receiving an explanation thereof. In any event, as stated in Applicant's November 30, 2006 Amendment, persons of ordinary skill would be able to differentiate between synthetic and natural components, if a need arose. Applicant believes that the methods for differentiation are known in the art.

For all the above reasons, Applicant submits that the objection to claim 104 is misplaced and requests withdrawal thereof.

If the USPTO continuous to object to claim 104. Applicant would appreciate a detailed explanation, supported by relevant sections of rules and/or statute, for the objection.

Claim Rejections under 35 U.S.C. §112, Second Paragraph

Claims 114-115, 129-130 and 138 were rejected as allegedly being indefinite because they lacked sufficient antecedent basis for the recitation of "grape seed extract" and "cartilage enzymatic hydrolysate". While Applicant disagrees with this rejection, in the interest of expediting prosecution, he amended the claims, which continue to be definite.

Claim Rejections under 35 U.S.C. § 103

Claims 104, 106, 108-115, 117, 120, 124-127 and 129-131 were rejected as obvious over the combined teachings of Kosbab (WO 00/07607) in view of Bombardelli et al. (EP, 0,659,402) (Bombardelli) and Hersh (U.S. Patent 5,906, 811).

In reply to Applicant's previous response, it was stated that

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> Applicant's claimed invention is drawn to a method to increase collagen synthesis or lessening the decrease in collagen synthesis via oral administration of a composition comprising one glycosaminoglycan from cartilage enzymatic hydrolysate, one polyphenolic, hydrophilic antioxidant present in grape seed and lycopene obtained from tomato extract. Applicant in arguments presented in the remarks filed 30 November 2006 and amendment filed 09 May 2007, however, repeatedly recites quantities of 'cartilage enzymatic hydrolysate'.
>
> Since invention is the subject matter defined by the claims, Applicant has to clearly state on the record the exact composition being orally administered in the claimed method to increase collagen synthesis in the dermis. Is it a glycosaminoglycan present in the cartilage enzymatic hydrolysate, or the cartilage enzymatic hydrolysate itself in combination with a polyphenolic, hydrophilic antioxidant present in grape seed and lycopene obtained from tomato extract that is being administered?
>
> Office Action, page 7.

At the outset, Applicant respectfully submits that his claim 104 requires at least one glycosaminoglycan and at least one polyphenolic, hydrophilic antioxidant present in grape seed. Claim 104, and all claims dependent from claim 104, recite lycopene, but all of them do not require the lycopene to be obtained from tomato extract. In particular, claim 104 does not have such requirement.

With respect to "cartilage enzymatic hydrolysate", Applicant respectfully submits that the claims prior to this amendment clearly defined the relationship between the claimed glycosaminoglycan and cartilage enzymatic hydrolysate; the herein amended claims continue to clearly define, such relationship as needed.

It was also asserted that:

> "Kosbab clearly teaches a method to enhance collagen production and maintenance thereof (i. e., the concentration of collagen does not decrease) in an individual via administering a composition comprising cartilage extract or chondroitin sulphate (i.e., a glycosaminoglycan), antioxidant (i.e., carotenoids, e.g., beta carotene, and flavonoids) containing plant extracts and lycopene (See Kosbab reference, Page 24, Lines 10, 20-2 1 and 24-25)."

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Office Action, p. 7.

Bonmbardelli was cited for its alleged teaching (at p. 6, ll. 47-53 and p. 7, ll. 1-4) of an orally administered composition comprising lycopene, beta-carotene and procyanidine oligomers from *Vitis Vinifera.* Hersh was relied upon for its alleged disclosure of a method to orally administer a composition comprising acerola extract, beta-carotene and proanthocyanidines grape seed extract. *Id.*

It was asserted that the motivation to combine the references was present in the references themselves, because Kosbab and Hersh teach orally administering a composition, which includes Applicant's claimed components, and Bombardelli substantiates the composition taught by Kosbab. Thus, it was concluded that Kosbab and Hersh teach a method for enhancing/maintaining collagen synthesis via oral administration to an individual in need thereof of a composition including the same components recited in the Applicant's claimed method, and pursuant to the same method steps as recited in Applicant's claims. *Id.*

Applicant respectfully traverses this rejection.

At the outset, it is respectfully pointed out that the initial burden of establishing a basis for denying patentability to Applicant's claimed invention rests on the United States Patent and Trademark Office ("Patent Office" or "USPTO"). *In re Fine,* 5 USPQ2d 1596 (CAFC1988), and *In re Piasecki,* supra. The USPTO failed to satisfy this burden for the reasons detailed below.

The combination of Kosbab, Bombardelli and Hersh is improper as a matter of law, at least because no reason was identified in the Office Action that would have prompted a person of ordinary skill in the art to combine elements of these three references to achieve Applicant's claimed invention. The U.S. Supreme Court recently reiterated that such reason must be supplied and conclusory statements are not a substitute for it. *KSR International Co. v. Teleflex Inc. et al.,* 127 S. C. 1727, 2007 WL 1237837 (U.S.), 82 USPQ2d 1385 (2007).

Applicant respectfully disagrees with the assertion in the Office Action that Kosbab "...clearly teaches a method to enhance collagen production and maintenance thereof ... in

an individual via administering a composition comprising cartilage extract or chondroitin sulphate (i.e., a glycosaminoglycan), antioxidant (i.e., carotenoids, e.g., beta carotene, and flavonoids) containing plant extracts and lycopene...", as allegedly disclosed at Kosbab's page 24, lines 10, 20-2 1 and 24-25.

Kosbab is directed to cancer protective and therapeutic compositions, as well as to protective and therapeutic formulas for the treatment of osteoporosis. *See,* e.g., page 2, lines 25-28 and page 4, lines 6- 8. In the passage at page 24 relied upon in the Office Action, Kosbab teaches Formulae II and III, which are "Specific cancer preventive and therapeutic formulas..." of his invention. *See* page 23, line 23 (emphasis supplied). Formula II includes, in pertinent part bioflavanoids. Formula III includes grape seed extract, antioxidant carotenoids, e.g., beta-carotene, lutein, lycopene, luteolin, zeaxanthin or apo-carotenal (beta-carotene being preferred) and chondroitin sulphate, among nine different types of ingredients, and a total of more than 25 specifically enumerated compounds.

However, as mentioned above, Kosbab teaches that Formulae II and III are cancer preventative and therapeutic Formulae, not a collagen production and maintenance formula, as was asserted in the Office Action. Applicant's claim 104 (and all claims dependent thereon) are directed to a method of increasing collagen synthesis or lessening the decrease in collagen synthesis in the dermis by administering to a human "in need thereof" the composition defined by the claims. Kosbab, conversely teaches administration of his Formulae II and III to persons in need of cancer prevention and cure. The lack of collagen production and maintenance efficacy of Formula III is underscored by the fact that Kosbab explicitly states that lycopene lacks such properties. See Table 2, page 32. If Applicant overlooked any passage of Kosbab that teaches the use of Formula III for collagen production and maintenance, Applicant respectfully requests the identification of such passage(s) by page and line number. (Besides bioflavanoids, Formula II does not appear to have any other ingredients that are relevant to patentability of Applicant's claims. Again, if Applicant overlooked any other pertinent portions of Formula II, identification thereof is solicited.).

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Thus, Kosbab does not disclose or suggest a method of increasing collagen synthesis or lessening the decrease in collagen synthesis in the dermis comprising the oral administration to a human in need thereof of a composition comprising:

> i) at least one glycosaminoglycan found in cartilage enzymatic hydrolysate, or synthetic form of at least one glycosaminoglycan;
>
> ii) at least one polyphenolic, hydrophilic antioxidant found in grape seed; or synthetic form of at least one polyphenolic hydrophilic antioxidant and esters thereof; and
>
> (iii) lycopene;
>
> wherein the weight ratio of the at least one polyphenolic, hydrophilic antioxidant to the lycopene is about 1:1 to about 200:1 and the weight ratio of the at least one glycosaminoglycan to the at least one polyphenolic, hydrophilic antioxidant is about 1:1 to about 200:1,

as is now recited in Applicant's claim 104.

The lack of disclosure or suggestion in Kosbab of Applicant's method is underscored by the fact that lycopene is not identified by Kosbab to have properties of increasing collagen synthesis or lessening the decrease in collagen synthesis. In Table 2, at page 32, lycopene is identified as having five different properties:

1. antioxidant to control oxidative stress;
2. regulate blood lipid levels and lipoprotein (A);
3. supplement deficiencies;
4. regulation and inhibition of homocysteine; and
5. anti-tumor/anti-cancer effect.

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While Formula III contains nine different categories of ingredients, comprising a total of more than twenty-five different specific compounds or categories, some of which include grape seed extract, lycopene and chondroitin sulfate, Formula III is specified by Kosbab to be used for cancer prevention and cancer therapy.

The lack of the *prima facie* case of obviousness based on Kosbab is buttressed by the fact that in his Table 2, there are at least 18 different ingredients having, according to Kosbab, collagen maintenance or collagen synthesis function, but lycopene is not one of them.

As discussed above, all such ingredients are disclosed within the context of "Cancer Formulations", see page 32. Thus, Kosbab teaches away from Applicant's claimed invention of claim 104. See, *Jansen v. Rexall Sundown Inc.*, 68 USPQ2d 1154 (CAFC 2003). (The court held that a patent claim directed to a method of treating or preventing pernicious anemia comprising administering to a human in need thereof a combination of vitamin B_{12} and folic acid was not infringed by administering the claimed vitamins in the claimed doses for a purpose other than treating or preventing pernicious anemia, at least because such a person would not have an intent to treat the pernicious anemia.) To paraphrase a well established rule (that which anticipates if earlier in time, infringes if later), Kosbab's disclosure, specifying lycopene as an ingredient not useful in collagen synthesis or lessening the decrease thereof, would have failed to render obvious Applicant's claim 104.

Bombardelli also fails to disclose or suggest a method for increasing collagen synthesis or lessening the decrease in collagen synthesis with any composition. Applicant agrees that Bombardelli discloses in his claims compositions which include lycopene, β-carotene and procyanidole oligomers, with procyanidole oligomers apparently being extracted from *Vitis Vinifera, Carmellia sinensis, Asesculus hippocastanum, Ginkgo biloba, Cardus marianum. See* page 6, line 46- page 7, line 4 of Bombardelli. However, Bombardelli's composition lacks glycosaminoglycan,

Significantly, Bombardelli states that his composition can be used in the prevention of physiopathological conditions related at least partially to overproduction of free radicals,

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particularly aging, atherosclerosis and cancer. *See,* Abstract. Such conditions are not synonymous with, or suggestive of, increasing collagen synthesis or lessening the decrease in collagen synthesis in the dermis of a human in need thereof. .

Hersh is directed to intra-oral antioxidant preparations used to prevent and ameliorate signs, symptoms and complications to oro-pharyngeal cavity and mouth from damage caused by free radicals species induced by tobacco smoke, smokeless tobacco or similar products. *See* column 1, lines 5-18. While Hersh's composition includes beta-carotene, proanthocyanidines from grape seeds and acerola, it does not include glycosaminoglycan and there is no suggestion in Hersh that his composition or method is directed to increasing collagen synthesis or lessening the decrease in collagen synthesis in the dermis.

In this context, Applicant respectfully disagrees with the assertion at page 7 of the Office Action that "...Kosbab and Hersh teach a method to enhance/maintain collagen synthesis via orally administering to an individual in need thereof a composition comprising same components and according to the same steps as are claimed in the instant method." Again, if Applicant overlooked any teaching or suggestion in Kosbab and/or Hersh that teaches such a method, Applicant would appreciate the identification of passage(s) of these references containing such teaching. Applicant explained in detail above why Kosbab and Hersh fail to disclose or suggest compositions having the same components as those in Applicant's claimed method.

Furthermore, please note that Applicant's claims now require that in his composition:

(1) the weight ratio of the polyphenolic hydrophilic antioxidant to the lycopene is about 1:1 to about 200:1; and

(2) the weight ratio of the at least one glycosaminoglycan to the at least one polyphenolic, hydrophilic antioxidant is about 1:1 to about 200:1.

Kosbab, Bombardelli and Hersh alone or in combination fail to disclose or suggest such ratios and the combination of such ratios.

For all the above reasons, the references fail to establish a *prima facie* case of obviousness of Applicants' claims.

Surprising and Unexpected Results

Even if, arguendo, the combination of the three references did establish a *prima facie* case of obviousness of Applicant's claimed invention (which Applicant strongly refutes), evidence of surprising and unexpected results of record in the application would rebut such *prima facie* case.

Applicant's Example 2 describes the effect of the claimed composition on collagen synthesis. The results demonstrate that cell cultures containing the polyphenolic, hydrophilic antioxidants and lycopene (GT in Table 2, page 20) exhibited a 25% decrease in collagen synthesis, relative to the control (no ingredients of the claimed invention). Cell cultures containing glycosaminoglycans and lycopene (FT) showed a slight increase in collagen synthesis, 4%, relative to the control. Cell cultures containing glycosaminoglycans and the polyphenolic, hydrophilic antioxidants (FG) showed a small increase in collagen synthesis of 14.6% compared to the control.

However, compositions comprising the glycosaminoglycans, the polyphenolic, hydrophilic antioxidants, and the lycopene (FGT) surprisingly exhibited a dramatic and unexpected 75% increase in collagen synthesis.

It is well established that all evidence of non-obviousness must be considered when patentability of the claimed invention is assessed, including "...comparative data in the specification in determining whether the claimed invention provides unexpected results". See *In re Soni*, 34 USPQ 1684, 1687 (CAFC 1995). Unexpected results must be established by factual evidence. *Id.*

Applicants included such evidence in the application and initially discussed it in the Amendment filed on November 30, 2006, and have again summarized it above. There is no

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indication in the July 30, 2007 Office Action that such evidence was considered. Applicant respectfully requests consideration of this evidence.

Applicant submits that proper consideration of this evidence rebuts any possible *prima facie* obviousness based on the three references and places all claims examined in the application in condition for allowance.

This evidence also refutes the assertion at page 8 of the Office Action that:

> the instantly claimed invention would have also been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the instant ingredients for their known benefit since each is well known in the art for the same purpose and also because of the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of each of the ingredients, *In re Sussman,* 1943 C.D. ***518.***

Applicant submits that the results presented in the application establishing the increase in collagen synthesis and/or lessening the decrease in collagen synthesis in the dermis by the claimed composition of Applicant's invention are not merely an additive effect obtained from each of the ingredients present in the composition. As demonstrated in Example 2, a composition comprising glycosaminoglycans, polyphenolic hydrophilic antioxidants and lycopene (as defined in (i), (ii) and (iii) of claim 1) surprisingly resulted in a dramatic and unexpected 75% increase in collagen synthesis. This is contrasted with a decrease in collagen synthesis of the composition which included polyphenolic hydrophilic antioxidants and lycopene and significantly smaller increases in collagen synthesis exhibited by the compositions comprising:

- glycosaminoglycans alone;
- glycosaminoglycans and lycopene;
- glycosaminoglycans and polyphenolic hydrophilic antioxidants.

This unexpected effect of the Applicant's claimed composition is not taught or suggested by the cited references (Kosbab; Bombardelli and Hersh) and could not have been predicted from the teachings of these references.

Kosbab, Bombardelli and/or Hersh, alone or in combination, provide no teaching or suggestion to those skilled in the art that the increased collagen synthesis or lessening in the decrease of collagen synthesis in the dermis can be improved by a method defined in Applicant's claim 1. Such a teaching or suggestion are required for a proper obvousness analysis, e.g. *In re Keller* 642. F 2d 413, 208 USPQ 871 (CCPA 1981).

Non-rejected Claims

Applicant notes that claims 136 and 137 were not rejected. Thus, Applicant understands that these claims are in condition for allowance. A confirmation of this understanding would be appreciated.

Conclusion

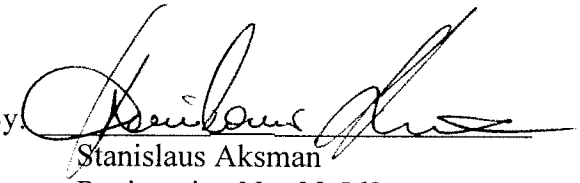
Applicant respectfully submits that for all of the reasons set forth above, the invention of claim 104 is *prima facie* patentable in view of Kosbab, Bombardelli and Hersh. Since all of the remaining rejected claims depend from claim 104, Applicant respectfully submits that they are also patentable in view of these references. Further, claims dependent from Claim 104 also contain additional recitations, and deserve separate patentability consideration.

In the event that any outstanding issues remain, Applicant respectfully requests the courtesy of a telephone call to the undersigned Counsel to resolve such issues in an expeditious manner and place the application in condition for allowance.

In the event that any variance exists between the fees enclosed herewith and those deemed necessary by the U.S. Patent and Trademark Office to enter and consider this Amendment and Response, or to maintain the present application pending, please credit or charge such variance to the undersigned deposit account number 50-2478.

Respectfully submitted,

Date: October 1, 2007

By: 
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